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10/083,283	02/23/2002	Laura L. Dugan	53047/31628	4140

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,283	DUGAN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12,15 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,15 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-12, 15 and 70 are presented for examination.

Applicant's request for reconsideration of the finality of the rejection of the last Office Action dated September 19, 2005 has been granted. The finality of the previous Office Action is hereby withdrawn.

Applicant's After-Final Amendment and Notice of Appeal filed December 16, 2005 have each been received and entered into the application. Accordingly, claims 2, 13-14 and 16-69 have been cancelled and claims 1, 3-12 and 15 are currently amended and claim 70 is newly added.

In view of the amendments and accompanying remarks, the rejection of claims 1, 3-12 and 15 under 35 U.S.C. 112, first paragraph, for insufficient enablement of C60 compounds; the rejection of claims 1, 3-12 and 15 under 35 U.S.C. 103(a) and the rejection of claims 1, 4-12 and 15 under the judicially created doctrine of obviousness-type double patenting have each been hereby **withdrawn**.

In view of the cancellation of claims 2, 13-14 and 16-69, the rejection of claims 2, 13-14 and 16, 18-30 and 56-67 under 35 U.S.C. 112, first paragraph; the rejection of claims 2, 13-14 and 16-69 under 35 U.S.C. 103(a) and the rejection of claims 13-14, 16-32 and 56-69 under the judicially created doctrine of obviousness-type double patenting have each been hereby rendered **moot**.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-12, 15 and 70 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for extending the lifespan of mice comprising the administration of the C60 compound *e,e,e* C60(C(COOH)2)2(CHCOOH); *e,e,e* C60(CHCOOH))3; C60(C(COOH)2)n and pharmaceutically acceptable salts, esters or amides thereof, does not reasonably provide enablement for extending the lifespan of mammals or mammalian cells in general using said C60 compounds, for the reasons already made of record in the previous Office Action dated September 19, 2005 at pages 2-9 and further in view of the following remarks made herein.

Response to Applicant's Remarks:

Enablement of Increased Longevity in Organisms Besides Mice

Applicant states that there is little support for the proposition that such claims are only enabled for the particular model system in which they are tested, since analysis of available case law indicates that the enablement requirement of 35 U.S.C. 112 for claims directed to asserted therapeutic uses is even satisfied in cases where the compounds were only tested in vitro or model in vivo systems (i.e., mice) and further relies upon the decisions of *Cross v. Iizuka* (753 F.2d 1040) and *In re Brana* (51 F.3d 1560). Applicant submits that actual testing outside of a

relevant in vitro or in vivo model system is not required to meet the enablement requirements of 35 U.S.C. 112, with respect to therapeutic uses, and that limiting the instant invention to the treatment of mice would set forth a standard of enablement for therapeutic methods that could only be met if the invention first passes through Phase II clinical trials involving human subjects. Applicant states that the mouse model system disclosed in the specification is a well documented system for identifying treatments that result in longevity increases and relies again upon the document "Interventions Testing Program" from The National Institute of Aging and Turturro et al. Applicant has also relied upon the fact that reductions in oxidative stress can result in lifespan increases even in non-mammalian organisms (e.g., *C. elegans* or *Drosophila*) would have led the skilled artisan to have ample basis for believing that the instant invention has enabled treatments for increasing the lifespan of other mammals.

Applicant's arguments have been carefully considered, but are not found to be persuasive in establishing error in the propriety of the present rejection.

The present rejection relies upon *In re Marzocchi et al.*, 169 USPQ 367 (CCPA 1971), which states:

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms *corresponding to the scope* to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support*; assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use

will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling." (emphasis added)

Applicant is also again directed to the MPEP at §2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern is whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of enablement involves the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to make and use the *entire scope* of the claimed invention without undue experimentation.

Questions of enablement involve consideration of the nature of the invention, the state of the prior art, and the level of skill in the art. The state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains.

The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification. The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date [*Chiron Corp. v. Genentech Inc.*, 363 F.3d 247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004)]. See MPEP §2164.05(b).

In the present case, Applicant's assertion and reliance upon *Cross v. Iizuka* and *In re Brana* in support of the assertion that there is little support for the proposition that the instant claims are only enabled for the particular model system in which they are tested has been carefully considered. However, as already stated above, questions of enablement are evaluated in consideration of the state of the prior art. It remains that the prior art was sufficiently unpredictable that a mere showing of results in mice would not provide a reasonable basis for extrapolating such results to any other, let alone all, mammalian systems.

It is in this regard that Applicant's attention is directed to *Ex parte Maas*, 9 USPQ2d 1746, which states, "Substantiating evidence may be in the form of animal tests which constitute recognized screening procedures with clear relevance to utility in humans. See *Ex parte Krepelka*, 231 USPQ 746 (Board of Patent Appeals and Interferences, 1986) and the cases cited therein." While Applicant has provided evidence in the form of animal tests (i.e., only in mice), the reliance on such evidence to support the utility of the present invention in humans, or other mammals, for that matter, is, respectfully, insufficient. Applicant has failed to establish, either in the present disclosure or the remarks submitted in response to the present rejection, that an experimental mouse model was recognized in the art as a model with predictive value in establishing efficacy of lifespan-extending therapies in humans or other mammals.

Applicant has relied upon the "Interventions Testing Program" from The National Institute of Aging (herein referred to as "NIA") in support of their position that mice are an art-accepted model of the activity of longevity therapies in humans. It is once again noted that the NIA reference conspicuously lacks any statement or express teaching that mice are the species most likely to provide information regarding such activity that could be translated to all

mammals, including humans, and merely teaches that the mouse will be used as a model to test a variety of different interventions to extend lifespan and delay disease and dysfunction. In other words, this reference does not support the assertion that mice are art-accepted models for extending lifespan, but rather only shows that they are the first step in testing.

Applicant states that, "Although the reference ["Interventions Testing Program"] provided may not explicitly state that mice will provide information that can be translated to humans, it is self-evident that the government would not support a program of this magnitude if there was not a reasonable expectation that the results obtained in mice could be extrapolated to other mammals and humans in particular." See Applicant's remarks at page 9. Government support for this program most certainly does not carry any weight in determining the predictive value of the results obtained in mice to the larger and highly varied genus of "mammals" or "mammalian cells". While government support may allow for continued experimentation in determining whether a mouse-aging model is reasonably suggestive of a human-aging model, such a fact has not been demonstrated and is still, according to the NIA reference, under investigation.

Thus, as stated in *Ex parte Balzarini*, 21 USPQ2d 1892, "There is no evidence of record that experimental animal models have been developed in this area which would be predictive of human efficacy." Applicant has failed to make an objective showing of evidence or sound scientific reasoning that would reasonably correlate the efficacy shown in mice to be an adequate projection of the same or substantially similar efficacy in humans or other mammals. While it is acknowledged that Applicants for patent are not required to reduce the invention directly to practice in a human model in order to claim the use of the therapy in humans, nor are they

required to progress to Phase II clinical trials involving human subjects, sufficiently persuasive and soundly scientific reasoning must be provided as to why one of ordinary skill in the art would reasonably extrapolate the results obtained in mice to the larger and highly varied genus of mammals in general. As discussed in *Ex parte Maas*, 9 USPQ2d 1746, "First, although Appellant's specification described certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical utility in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to utility in humans or animals." (emphasis added) In the present case, a person having ordinary skill in the art would have been highly skeptical to extrapolate the results shown in mice to all mammals, including humans, particularly in the absence of any scientific basis for such an extrapolation.

Applicant fails to address the considerable differences between those animals contained with the huge genus of mammals in general. The term "mammals" is inclusive of more than 5000 species placed in 26 orders (see "Animal Diversity Web", first paragraph at page 1), and can generally be divided into three categories based upon their reproductive condition: (1) Prototheria, or monotremes, which lay eggs (i.e., the platypus), (2) Metatheria, or marsupials (i.e., the kangaroo), or (3) Eutheria, or placental mammals (i.e., humans) ("Animal Diversity Web", first paragraph at page 5). While mammals as a general class share some distinctive characteristics not found in other animals, such as middle ear bones, hair and lactation via mammary glands ("Animal Diversity Web", first paragraph at page 2), the general class of mammals contain a vast diversity of forms, ranging from the smallest known mammals, such as

shrews and bats, to the largest known mammal, such as the blue whale ("Animal Diversity Web", second paragraph at page 2), and further exhibit a diversity of developmental and life history patterns that vary among species and larger taxonomic groups ("Animal Diversity Web", first paragraph at page 5). In addition, it is known in the art that mammals vary greatly in lifespan, where small mammals such as mice may live a matter of days or months, whereas bowhead whales may live more than 200 years ("Animal Diversity Web", fourth paragraph at page 7).

Thus, mice alone would represent $\leq 1/4500^{th}$ of the class of mammals (i.e., <0.02%). Extrapolation from 0.02% for the entire class of mammals would not be considered enabling in view of the different biology of each subclass, let alone each animal within each subclass. Furthermore, the usual lifespan for mice is, at best, $\leq 1/40^{th}$ the lifespan of a human, and even less when compared to, for example, an elephant or a whale, each of which has an extremely long lifespan.

The current application disclosure does not present any guidance necessary to permit one skilled in the art to extrapolate the teaching with regard to mice to each of the classes of mammals and to the species contained therein. For example, the current claims recite extension of up to 32%, but a direct ratio of lifespan results in astounding values. For instance, the longest living human was Jeanne Louise Calment (b. 1875, d. 1997), who lived to the age of 122 years (see www.wonderquest.com/LifeSpan-MaxMin.htm). Extension of life by approximately 30% as presently claimed would have meant that Calment would have lived for about 159 years (122 x 1.30=159 years), or an extra 37 years. If that were the case, Calment would still be alive at the present time.

Applicant states on the record that the presently claimed process is capable of extending lifespan about 32% "beyond the generic expected lifespan for said mammal or mammalian cell". However, the lifespan of, for example, a mouse (i.e., for the purpose of discussion, approximately 23.5 months as demonstrated by Applicant's control population of mice), is distinctly different than that of a human (i.e., approximately 80 years), which is also distinctly different that a bowhead whale (i.e., more than 200 years). Although Applicant has claimed a 32% (Applicant's internet site indicated <32% extension; see http://medicine.ucsd.edu/geriatrics) extension of lifespan in any mammal based on the activity in mice, it is noted that the extension of lifespan by a matter of a few months is not reasonably suggestive of extending lifespan by, say, 25+ years. A reasonable interpretation of Applicant's subject matter would indicate that Applicant allegedly claims to be able to extend a human life by about 32%, or about 26 years, to approximately 106 years of age, or even to extend the life of a bowhead whale also by about 32%, or about 64 years, to approximately 264 years of age. Such an assertion is sufficiently unusual that the skilled artisan would not have been imbued with at least a reasonable expectation of success that one single active fullerene agent would have shown such efficacy in extending the lifespan of a human or any known mammal or mammalian cells, given that the only results in support of such a claim demonstrate an extension of lifespan in mice by approximately 5 months. In other words, the invention would be claiming an outcome that would not have been reasonably expected by the skilled artisan.

In support of the claim that the data presented in the instant specification regarding increased longevity in mice is sufficient to reasonably extrapolate to all mammals or mammalian cells, Applicant has also relied upon the Turturro et al. reference.

Reliance on Turturro et al. also fails to support Applicant's extrapolation of the results demonstrated in mice to all mammals or mammalian cells in general. Turturro et al. states, "It was also intended that any panel of rodent-aging biomarkers would also provide some basis for developing biomarkers of aging in humans. This was based on the assumption that biomarkers useful across different genotypes and species would be sensitive to fundamental processes that would extrapolate readily to humans." (see page B492, first paragraph of column 1) While it is acknowledged that Turturro et al. speculates that the biomarkers identified in rodents would be readily extrapolated to humans, Turturro et al. expressly states that such is an ***assumption*** and is not fact. Furthermore, the remainder of the discussion of Turturro et al. fails to draw any conclusions regarding the equivalence of the biomarkers found in rodents to those potentially found in humans or other mammals.

In further response thereto, the study on which Turturro et al. is based discusses the differences in lifespan and food consumption, namely the extension of lifespan seen when the animals were fed ad libitum versus the extension of lifespan seen when the animals were fed using caloric restriction. It does not discuss, even in a tangential way, the administration of fullerene compounds, particularly those presently claimed, as a possible means for extending lifespan. Therefore, Applicant's reliance on such a document to properly conclude that a rodent-aging model is predictive and suggestive of the same or substantially the same activity as in a human-aging model is flawed. The disparate nature of the treatment used in Turturro et al. (i.e., natural dietary modifications) versus the treatment used in the present claims (i.e., C60 fullerenes) does not lend itself to be suggestive or predictive of the activity of C60 fullerene

compounds in a rodent model, let alone to support the contention that the activity of any agent in a rodent model is suggestive or predictive of the activity of such an agent in a human model.

Moreover, Applicant has relied upon the fact that the demonstration of reductions in oxidative stress can result in lifespan increases even in non-mammalian organisms such as *C. elegans* or *Drosophila* and that, in light of such, the skilled artisan would have ample basis for believing that the instant invention has enabled treatment for increasing the lifespan of other mammals. However, to conclude that the skilled artisan would have believed that the instant invention is enabled for extending the lifespan of other mammals merely based on the fact that it is an effective catalytic antioxidant capable of extending lifespan of mice, and that reductions in oxidative stress have been shown to result in an increase in lifespan in non-mammalian organisms, is fundamentally flawed. Lifespan-extending activity of an agent demonstrated in non-mammalian organisms is most certainly ***not*** suggestive of the activity of the same agent in mammals, if only because mammals are significantly more complex than their non-mammalian counterparts in structure and function and would, therefore, be expected to react differently in a mammal versus a non-mammal. In addition, simply because reductions in oxidative stress may have had lifespan-extending properties in some mammals is also most certainly ***not*** suggestive of the same activity in all types of mammals or mammalian cells since the variety and disparate nature of the animals encompassed by the term "mammal" is sufficiently different that any activity shown in one type of mammal would not be predictive of the same or substantially similar activity in another type of mammal.

For example, Applicant discusses several studies at pages 3-4 of the present disclosure of the use of deprenyl for increasing the lifespan of rats, Drosophila and humans. However, while

the studies in rats demonstrated a potential increase in longevity (see paragraph bridging pages 3-4 and first full paragraph at page 4 of the specification), the use of deprenyl for treating humans with the objective of increasing longevity showed conflicting results, such that some patients showed an increase in survival and other patients showed increased mortality. Such results cast significant doubt as to whether the activity of an agent in increasing lifespan in mice would have been reasonably suggestive of the same or substantially similar activity of the same agent in a human, since it has already been demonstrated in the art that such is not necessarily the case. By extrapolation, one skilled in the art would conclude that no one compound would have uniform effects. Of note is that the current application appears to have conducted studies in one line of mice, but there are several other lines of mice for which no comparative data are presented.

It is noted that Applicant has not provided any persuasive evidence or argument other than the reliance on NIA and Turturro et al. in the present disclosure or in the response to the rejection made under 35 U.S.C. 112, first paragraph, as to how the example and data shown in the specification is reasonably representative of the ability to extend lifespan in a mammal or mammalian cell ***in general***. In consideration of the fact that the specification fails to provide sufficient reasoning or support for why the data demonstrated in the disclosure would be logically extrapolated to the treatment of all mammals or mammalian cells in general other than Applicant's own assertion thereof, and, further, in light of the fact that the state of the art with regard to the treatment of such conditions is highly complex and poorly understood as stated at pages 3-9 of the previous Office Action dated September 19, 2005, it remains that the specification is viewed as lacking an enabling disclosure of the same.

It is reiterated that the demonstration of enabling results in one species of more than 5000 known species of mammal is, respectfully, not sufficient to entitle Applicant to assert that such is reasonably representative of all known mammalian species. Applicant is again reminded that the only relevant concern regarding the breadth of claims with regard to the enablement requirement is whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. Please reference MPEP §2164.08. It is obvious that the enablement of one species by the disclosure is clearly not commensurate in scope with what is presently claimed (i.e., all mammals or mammalian cells in general).

It is in this regard that Applicant's attention is further drawn to Figure 4, upon which Applicant has relied to demonstrate that the presently claimed process is capable of extending lifespan up to 32% based upon the fact that one mouse was still alive at 33 months. While such survival has been noted, only ***one*** of the nine mice receiving C3 treatment lived beyond the mean 28.7 (~29 months) month survival point to 33 months. The majority of the studied mice (8/9) did not show the same survival characteristic of this one mouse. Thus, the fact that Applicant has claimed that the presently claimed process is capable of extending lifespan up to 32% is not based on the results demonstrated by a majority of the studied mice, but rather is based simply upon the results obtained in only one mouse. While the importance of such a result is not diminished in the present discussion, it is noted that the extension observed in one mouse is not reasonably representative of the overall amount of extension seen generally in the other remaining mice, nor is it statistically demonstrative of lifespan extension of other species of mouse or other mammals.

Applicant has compared the individual survival results of one mouse to the mean survival results of the control mice. However, such a comparison is not scientifically sound, considering that the mean survival obtained in the control mice has averaged out all data points and, therefore, the significance of some "outlying" data points, i.e., those that showed a higher rate of survival than the majority of other mice, has been diminished. A statistically sound comparison of the data obtained in the study would have been to compare the mean survival of the C3 treated mice, which according to Applicant's specification includes the mouse still alive at 33 months (see page 10, lines 10-12 of the present disclosure), and the control mice. Such a comparison would have determined the increase in the rate of survival to be approximately 22% (i.e., (28.7-23.5)/23.5=0.22), not 32% as presently claimed, and which is in keeping with Applicant's statement of the results at page 21 of the present specification, which states, "The results of these experiments are displayed in Figure 4 and show a marked increase (approximately 20%) in the lifespan of mice."

Respectfully, it is also noted that Applicant has appeared to ignore the fact that one of the control mice lived to 32 months, which casts doubt on the statistical significance of the continued survival of the one C3 treated mice that lived to 33 months, since it does not show a marked difference between the greatest survival seen in the treated group and greatest survival seen in the control group.

Applicant's attention is directed to the newly cited document, "Biology of Aging and Reactive Oxygen Species" (http://medicine.ucsd.edu/geriatrics), at page 2 under the heading "Translational Research on Fullerene Derivatives and Neuropharmaceuticals and Anti-Aging Agents". Studies by Dr. Dugan using the same compound C3 in mice were shown to extend the

lifespan of the studied mice by approximately 11%. Such an extension is also in direct contradistinction to the 32% lifespan extension presently claimed. Once again, considering what was known in the art, namely that the compound C3 was shown to be capable of extending the lifespan of mice by 11%, to now claim that the same compound was capable of extending the lifespan of mice by 32% would have been an outcome that would not have been reasonably expected by the skilled artisan. In light of such, the degree to which Applicant must enable such results is much higher than if Applicant were claiming an outcome that would have been reasonably expected by the skilled artisan. Respectfully, it appears that Applicant has not adequately met this burden.

Furthermore, Applicant has not made it clear on the record as to how the control mice and the C3 treated mice as depicted in Figure 4 were fed. In particular, it is not known whether the studied mice were subjected to caloric restriction diets or whether the mice were fed ad libitum. Calorie restriction was a process well known in the art as a method of inhibiting the aging process and thereby extending lifespan in this animal. In this regard, Brack et al. ("EMBO Workshop Report: Molecular and Cellular Gerontology", 1999) is cited. "Calorie restriction is one of the few regimes that positively influences most aspects of aging in all organisms tested so far. Brian Merry (Liverpool, UK) reported on the positive effect calorie restriction has on the lifespan of rodents, Rhesus monkeys and squirrel monkeys. In rats, calorie restriction alters the rate of aging, resulting in life extension. When these calorie-restricted animals are refed normal diet, aging is again accelerated." (see Brack et al., middle paragraph at column 1 at page 1932). Thus, Applicant has not clearly delineated on the record if any of the studied mice were fed via a calorie-restricted diet. If such was the case, Applicant would need to show what portion of the

extended survival effect would have been attributable to the diet alone and what portion would have been attributable to the fullerene compound alone.

Applicant has also noted that the C57B6NIH mice employed in the Experimental Study of Example 2 (see page 21, for example, of the present specification) were not selected in any way for health, tumors or other disabilities. However, while the mice may not have been specifically selected for any type of "disability", it has not been made clear on the record whether Applicant considered the fact that the studied mice may have had other genetic mutations that may have contributed to or retarded against increased lifespan in the mice. Applicant expressly states at the paragraph bridging pages 4-5 of the present specification, "Several genes in mice have been identified as 'longevity' genes because mice with mutations in these genes have greater mean lifespans relative to the expected lifespan control mice. These genes include the Ames dwarf mutation, and the Snell dwarf mutation. However, these mutations result in small, frail mice, which have difficulty feeding. It is believed that the longevity conferred by these mutations is essentially due to calorie restriction. Recent attempts to use gene array analysis, or other genetic screens for genes associated with longevity phenotypes in worms, flies and rodents have come up with a number of candidate genes. In general, however, they are frequently 'stress-response' genes." Absent factual evidence to the contrary, it appears that Applicant did not consider what effect, if any, the genetic makeup (i.e. genetic mutations) may have had on the survival of the mice studied.

Therefore, in the absence of such considerations, such as the diet on which the mice were fed, and the analysis of the genetic makeup of the mice, Applicant's results cannot be afforded the same significance as an enabling disclosure as Applicant has requested, since Applicant has

not clearly delimited what effect the presently claimed fullerene agents actually have on the extension of lifespan in the absence of other lifespan-extending contributing factors, such as diet or genetic makeup.

For these reasons, and those already made of record at pages 2-9 of the previous Office Action dated September 19, 2005, rejection of claims 1, 3-12, 15 and 70 for failing to meet the enablement requirements of 35 U.S.C. 112, first paragraph, remains proper and is **maintained**.

Conclusion

Rejection of claims 1, 3-12, 15 and 70 is deemed proper and is **maintained**.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-5:00 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leslie A. Royds
Patent Examiner
Art Unit 1614

January 23, 2006

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